Historic discovery of natural thermodynamic cause of cancer

Dariusz Jasiczek [1], Irena Kaim [2], Krzysztof Czajkowski [3]

1 Fertility Centre, Cracow Poland
2 Collegium Medicum Jagiellonian University, Cracow, Poland
3 Warsaw Medical University, Warsaw Poland

Correspondence to: Irena Kaim, MD.
Department Obstetrics and Perinatology CMUJ
Kopernika 23, 31-501 Cracow Poland.
e-mail: ikaim@cm-uj.krakow.pl

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Abstract

The essence of life is best manifested in cell, which, when brought to the edge of its existence in the actual environment may and sometimes must self-organise into an entirely different cell (neoplasm), but it must enhance dissipation of matter and energy in its closest environment. This phenomenon has been described before as self-organisation of dissipative structures in physics, chemistry and even sociology. Each neoplastic cell is such a dissipative system – with its clonal growth, the cell causes increasing disorganisation of the body, in consequence leading to neoplastic disease. The only adequate cause of formation of neoplasms is an internal dissipathogenic cellular state, which is clinically identify as preneoplastic ones at the level of morphology or molecular biology but also biophysics.
Two general directions for therapy of neoplastic diseases arise from the thermodynamic essence of neogenesis: the direct one – targeting neoplasms, and the indirect one – leading to normalisation or sufficient alteration of their environment. The greatest disappointment in the fight against neoplasm was the discovery of its thermodynamic cause in a natural self-organisation of biological dissipative structures. It is this dissipation that causes the signs and symptoms of neoplastic diseases ending with destruction of the body if the treatment comes too late and/or is insufficient, limited only to removal of neoplastic lesions without the always necessary elimination and/or prevention of preneoplastic (dissipathogenic) states.

REVIEW ARTICLE

INTRODUCTION

Cancer is a colloquial term for hundreds of terminal diseases destroying the body in their final phases and usually occurring unexpectedly at any time of human life. Despite the similarities between them, until the end of the 20th century the diseases were not expected to have the same cause, which is why there were attempts to assign an individual source to each of them, and in 1926 J. A. Fibiger was even awarded the Nobel Prize for discovering *Spiroptera neoplatsica*. Many carcinogenic factors were also described, including naturally occurring genes, which were even given a name 'oncogenes.' Social damage was also done by the forecast announced in 1971 that incidence of cancer would be reduced by half before the end of the 20th century and afterwards cancer would be eliminated. At the same time its ominous nature was highlighted, which only increased the fear

of the disease. Finally, the ambiguity of 'cancer' as the term for both the neoplasm and the neoplastic diseases it caused became common also among physicians (Czajkowski 2009; Fedor-Freybergh 1992; Hodorowicz *et al.* 2011; Jasiczek & Klimek 2011; Kaim *et al.* 2001).

Health means an inner state of human body in which equilibrium of its components (microsystems) and the relationships between them prevents man from contracting a disease, that is from losing the stability of the body and ensures exchange of matter, energy and information with the surroundings. In humans these impacts pertain not only to matter and energy but they are also mental and emotional. A disease is a manifestation of loss of this inner equilibrium on the branch of possible stable body states, which characterises each system. Man recovers more easily in a state close to the inner equilibrium than in states that are more distant from it, which eventually precede death of the body in the point ending the personal branch of the possible forms of its existence. This is when man dies as a system, even though his cells, tissues and even whole organs may, as microsystems, function in the system of another person after being transplanted.

The cellular form of life is the dividing line separating clinical practice from theoretical medicine, at the same time being the basis for understanding etiopathogenesis of neoplasms. Living systems are characterised by life as a spontaneous, mutual exchange – referred to as bio – of matter, information and energy, conditioning their existence as one whole, being more than just the total of their components and the relations between them. The essence of the life hidden in them can be fathomed through various form of its manifestation (Klimek 2007b, 2010). Once denatured, the simplest biochemical compounds (proteins, viruses) lose their biological hormonal or enzymatic functions without changes to their chemical composition. However, they cannot replicate by themselves, contrary to e.g. viruses, achieving it using higher forms of life such as cells, which in favourable conditions are able to divide on their own into daughter cells due to their ability to exchange matter and energy with the environment. By forming tissues and organs, cells perform additional external work for the benefit of adjacent cell structures. In the end, life reaches even higher forms as independent multi-cellular organisms and finally – people, to be eventually captured in an apparently non-material form of social life (Klimek 2001, 2004; Klimek *et al.* 2011).

The essence of life is best manifested in cell, which, when brought to the edge of its existence in the actual environment (surroundings), may – and sometimes must – self-organise into an entirely different cell (neoplasm), with a new genetic identity. This phenomenon is universal and it has been described before as self-organisation of dissipative structures in physics, chemistry and even sociology. In special circumstances, life of a cell condemned to death may be saved through exchange of matter – even that of its own, non-functional organelles – into energy, on condition that such a new cell, due to improved metabolism, may still function; however, what is most important, it must enhance dissipation (diffusion) of matter and energy in its closest environment. Yet, it need to be borne in mind that by changing the genome a cell receives an identity different than that of the rest of the body, which is the only one it can exist in, and this is why it condemns itself to death together with the body as its own neoplastic clone develops (Klimek 1980, 1982, 1983, 1985a,b, 1990a,b,c,d, 1992). Even though it has been thirty years since this thermodynamic cause of cancer was discovered, many physicians still have not adapted to this new interpretation of cancers, which unfortunately applies also to specialised oncologists, who, fortunately, have been using spectroscopy and organ imaging with Nuclear Magnetic Resonance with increased frequency. Three-dimensional images of the inside of a body are an outcome of recording billions of resonating atoms and particles, with their matter and energy states also taken into account, which requires not only understanding of the technology of the medical devices used, ultimately presented in their user manuals, but first and foremost it pertains to the necessary replacement of a diagnostic and therapeutic procedure with one that is in accordance with new terminology. Just like man loses strength and good health simply as a result of aging, at the roots of all phenomena such useless loss is referred to as entropy and treated as the measure of chaos (disorder) of every system. The more disorganised the system, the greater the losses. The notion of entropy is incredibly important with reference to biological systems (e.g. organism, cells, cell nucleus, or cell cytoplasm) since according to the second law of thermodynamics, the total value of entropy increases in a system and its environment must always be positive. If for any reason a cell reduces production of its own entropy, it must increase it in its environment through the most generally perceived diffusion (dissipation) of matter and/or energy. Each neoplastic cell is such a dissipative system – with its clonal growth, the cell causes increasing disorganisation of the body, in consequence leading to neoplastic cachexia (Figure 1)

Independent life of a neoplastic cell turns out to be more important than its hitherto existence, a phenomenon in single-celled organisms referred to as mutation, i.e. better life adaptation to the extremely unfavourable environment (surroundings). Inseparable matter- and energy-related aspects of cell metabolism are governed by the genome of the cell nucleus and by nucleic acids of mitochondria, which are directly influenced by various types of energy, such as heat and cold, light and sound, atmospheric pressure, gravity and movement. In the multi-cellular body of man, there is additionally a bioenergy connected with emotions, religion, fear, beliefs and ideology, as well as such matter-related factors as air components, food, saprophytic and pathogenic microorganisms and their toxins. At the moment of death,

the psycho-neuro-immuno-hormonal regulation of the inner state of the whole body disappears, even though the cells that form it may stay alive for a long time after that and a tissue or organ form of life may even function as a transplant in a biologically similar body of the recipient. The life of man and the accompanying microorganisms as species is, however, something different than the always single, i.e. unique clone of one neoplastic cell, unable to live independently as a species. Neoplasms very rarely outlive their hosts, unless they are provided with the right existence and cloning conditions in a cell culture (Jasiczek & Klimek 2011; Klimek 2001b; 2006).

In a multi-cellular organism, many cells (microsystems) die all the time to ensure that the system is whole despite the impact of ageing processes and pathogenic stimuli. The end of their life may be in exceptional cases prevented by self-organisation into a new creation (system), which again begins its own thermodynamic branch of possible stable inner states with the equilibrium. This phenomenon, universal in nature, discovered by Ilya Prigogine (Nober Prize 1977) (Prigogine 1980), was used by Rudolf Klimek to explain the reason for formation and diversity of neoplasms as biological dissipative structures, even despite simultaneous existence of the same cells of the body (Klimek 978a,b, 1980, 1982, 1983, 1985a). Each dissipative structure is formed as a result of statistically conditioned processes and this structure is only one of the numerous systems that may self-organise, hence so many types of cervical or breast cancers, even if diagnosed at the same time in one and the same person. The only adequate cause of formation of neoplasms is an internal dissipathogenic state of a cell resulting from many varied but necessary factors. A neoplastic cell is always strictly isolated from the body cells that surround it, even those in a dissipathogenic state, which we clinically identify as preneoplastic states – and not only at the level of morphology or molecular biology but also biophysics, if we are to mention imaging and spectroscopy using Nuclear Magnetic Resonance (Kaim *et al.* 2001, 2005; Klimek 1987b, 2001a,b,c).

NEOPLASMS AND NEOPLASTIC DISEASES – HISTORICAL OVERVIEW

The very term "neoplasm" expresses its most distinctive feature, i.e. its de novo formation in a multi-cellular organism as a self-regulating dissipative structure dispersing energy and matter. This is a natural phenomenon, governed by the same thermodynamic laws of Nature regardless of the size and type of the participating systems, each with its own, separate environment. This, however, does not mean reductionism of

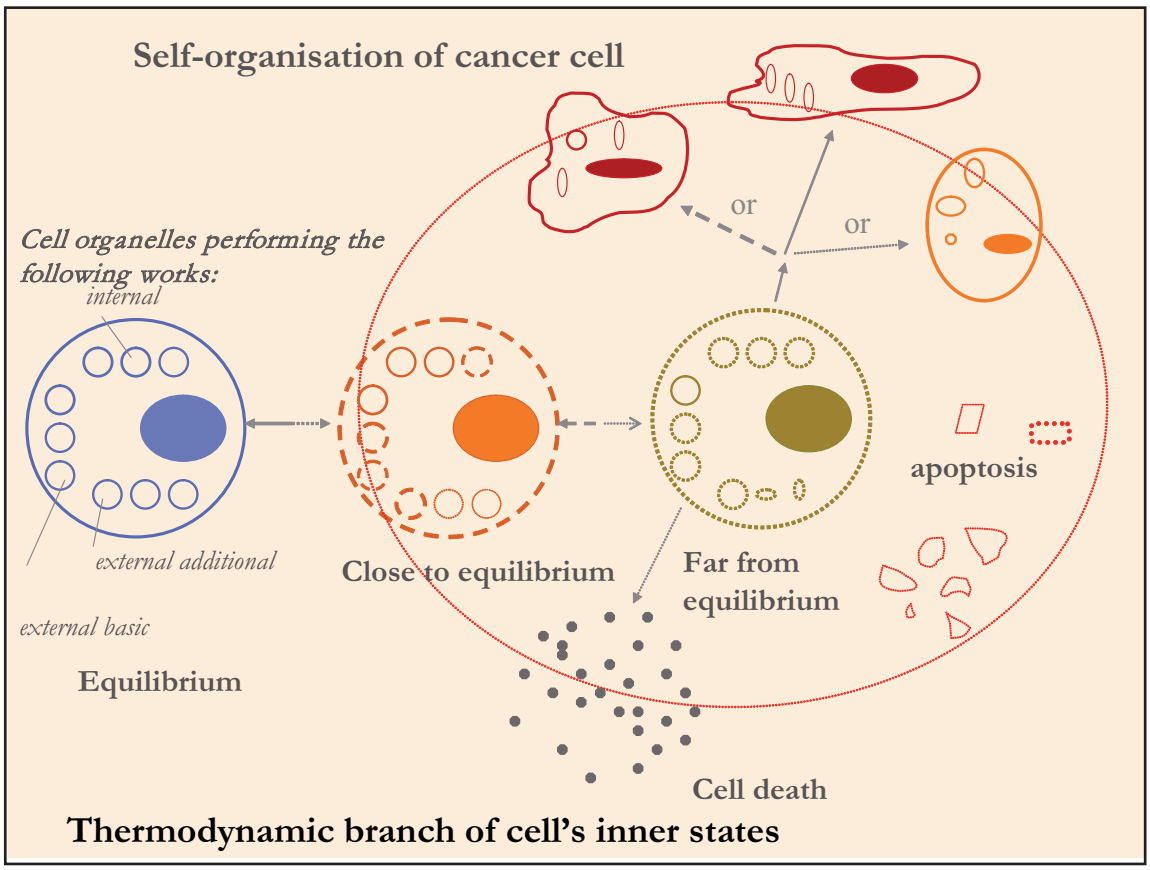

Fig. 1. A dissipative system of neoplastic cell.

the structure of human body to atoms, as many falsely think, but this means carcinogenesis of increasingly efficient systems, from formation of new chemical particles to construction of satellite cities around large agglomerations or social revolutions. The thermodynamic theory of neoplasms was confirmed once imaging using Nuclear Magnetic Resonance was introduced in the USA (Klimek *et al.* 1981a,b, 1982a,b; Mann *et al.* 1984). This was also documented in the fact of awarding honorary doctorates to two later Noble Prize winners: A. V. Schally (1976) and P. Lauterbur (1988); furthermore, this standpoint, being an outcome of one-hundred-year-long studies at the Jagiellonian University in Cracow, was not questioned (Klimek 1990a,b,c,d) in the international evaluation of the paper *Etiopathogenesis of tumors and theories of oncogenesis* (Klimek 1983).

In 1906, the position of the head of the Department of Biochemistry at the Jagiellonian University was given to Leon Marchlewski, who gained recognition in the world of science for demonstrating the haematoproteid structure of plant chlorophyll and animal haemoglobin. His student and his successor from 1946, Bolesław Skarżyński, confirmed this unity of Nature by discovering estrogens in willow flowers in 1936 and complemented this direction of studies with a statement that Nature solved many problems using the same components (microsystems). He explained that twenty-odd letters of the alphabet were used to form an endless number of words and still all possibilities had not been exhausted. In 1956, together with his students Rudolf Klimek and Tadeusz Szczepkowski, he demonstrated that self-feeding chemosynthesisers Thiobacillus thioparus drew energy from sulphur transformation, using also haemato-proteid cytochrome S, analogical in structure to cytochrome C of animal cells and cytochrome F of plant cells (Klimek 1956; Skarżyński, 1956). Between 1957 and 1967 R. Klimek introduced treatment using hypothalamic hormones to medicine, thus explaining e.g. the neuro-endocrinological determinant of cervical cancer. A. V. Schally and R. Guillemin received the Noble Prize for isolating and synthesising these hormones in 1977 (Klimek 1964, 1978a, 1985b; Klimek & Paradysz, 1969; Klimek & Pawlikowski, 1973). Together with J. Madej, he described a different reactivity of blood vessels to those hormones in neoplastic and preneoplastic cervical states and the frequent co-morbidity of clinical postpartum hypothalamic dysfunction (hypothalamic insufficiency) as a factor predisposing a patient to neoplastic lesions (Klimek 1978b; Klimek & Madej, 1964, 1985). Together with Marek Pawlikowski, he developed the first clinical textbook in the world, entitled *Clinical Neuroendocrinology* (published by PZWL, Warszawa) as early as in 1972, just after the structure of the first hypothalamic hormones had been learnt, which brought molecular biology closer to psychology (Klimek & Pawlikowski, 1973).

In 1906, professor of the Jagiellonian University Marian Smoluchowski described the foundations of the kinetic theory of matter and stochastic processes, including the one currently known as the Einstein-Smoluchowski fluctuation-dissipation theorem, thus explaining the role of thermal fluctuations in optimisation of the functioning of living systems and dispersion of light in opalescence (Smoluchowski, 1906). This thermodynamic depiction of events in the morphology-dominated medicine initiated a new direction for function tests, even though at that time Rudolf Virchov's cell theory of the structure of man was not fully accepted. The relationships between morphology and function with regard to neoplastic diseases were appreciated in 1942 by B. Skarżyński, who – together with the Noble Prize winner (1929, in chemistry) H. von Euler-Cheplin – wrote *Biochemie der Tumoren* (1942, F. Enke Verlag, Stuttgart, translated to Italian in 1945 r. La biochemica dei tumori, Einaudi, Torino), which initiated the biochemistry era in oncology, following the previous periods of dominance of pathomorphology and epidemiology in medicine (von Euler-Cheplin & Skarżyński, 1942). In five chapters: I. *General biology of neoplasms,* II. *Transformation of matter in the body of a patient with cancer.* III. *Formation of malignant tumours;* IV. *Suppression and withdrawal of tumours, neoplasms* and V. *Chemical diagnosis of cancer*, the authors discussed the impact of hormones on the development and formation of tumours in experimental studies and gathered the facts pertaining to biochemistry of viruses, mutation and formation of neoplastic cells through radiation and chemical stimuli, among other matters. Thy connected the aetiology of neoplasms with cell nucleus and gene and its mutation as the new starting point for cancer research. They decided that the gene responsible for heredity is a nucleoproteid, but at that time its exact structure was unknown. There is a modern ring to their statements that a "*cancer cell is a mutated cell and diet creates favourable conditions for development of cancer*" along with the suggestion that lifestyle and nutrition may help fight the neoplastic disease!

Between 1953 and 1955, B. Skarżyński generalised his own oncological views in papers "Chemism of carcinogenesis" and "Biochemistry of Neoplasms," stating that: "*Chemical research on neoplasms, conducted for over 50 years, have been assuming that by showing the differences in the chemical composition between normal tissues and neoplastic tissues, as well as the differences in the chemical processes taking place in a cell of neoplasm, one can explain the essence of cancer formation. This research led to accumulation of incredibly rich factual material but failed to answer the fundamental questions asked by a clinical oncologist. All attempts to identify in neoplasms a specific chemical compound, typical only of a neoplastic cell and absent in a normal cell, have failed. The differences between a normal tissue and neoplasm are only quantitative rather than qualitative. The ratio of individual protein fractions in the growing neoplastic tissue is changed but such changes take place also in foetal tissue and in regenerates – the most characteristic*

chemical features of a neoplastic tissue can possibly be demonstrated in the area of proteins and nucleic acids." (Czajkowski, 2009; Kaim *et al.* 2001)

Professor B. Skarżyński studied the mechanism of carcinogenic effects of diazo dyes, which by combining with proteins in a liver cell block its normal metabolism. This may lead to formation of a cell that is able to live but has a changed metabolism, as a result of adapting to the altered conditions. "*Such a cell either is already neoplastic or transforms into a neoplastic cell under other, non-specific factors. Inhibition of these proteins, their exclusion from normal cell metabolism and the consequent formation of new types of cells with different properties – it is a theoretical conclusion that can be drawn from the experimental material gathered.*" Guided by his rich experience and creative intuition, he captured the pathomechanism of neoplasm in two sentences: "*A significant moment in the transformation of a normal tissue into a neoplastic one is such damage to cells that does not make the cell unable to live but that is sufficient to alter its metabolism in a specific way. According to these facts accumulated by biochemistry, carcinogenesis would be a response of a normal tissue to continuously repeated minor damage, to unfavourable environmental conditions created by a carcinogenic factor.*" This statement could be fully explained only at the level of biophysics. In 1977 Rudolf Klimek, using the universal phenomenon of self-organisation of dissipative structures, explained etiopathogenesis of neoplasm, a sufficient reason for the formation of which is a dissipathogenic state of cell (Klimek 1978a,b, 1980, 1982, 1983, 1985a). This way he introduced to medicine the need to consider energy changes equally with biochemical and structural changes, which gave rise to oncological thermodynamics. He was the first to define cancer as: "*a natural biological dissipative structure self-organising in the body; if a part of the body (microsystem) is for a sufficiently long period in a state far from the biological equilibrium of its environment, and the body as a whole cannot change this state to one that is at least close to the equilibrium, than such a microsystem has an alternative: to die or to choose the lesser of two evils and transform into a new biological structure (a new system), that is a neoplasm. Carcinogenesis is the rarest but the most dangerous consequence of provoked disruptions of the internal state of the system and at the same time a signal warning against the endangered existence of the whole body; prophylaxis of neoplasm ought to involve elimination of all deviations from the equilibrium, especially at the level of the whole body.*"

CONFIRMATION OF THE DISSIPATIVE ESSENCE OF NEOPLASM

In 1980, R. Klimek together with P. Lauterbur (chemist) and M. H. Mendonca-Dias (physicist) generalised the results of independent studies in a publication about relaxation times of Nuclear Magnetic Resonance in neoplasms within their interpretation as self-organising dissipative structures and their *in vivo* studies using zeugmatographic NMR visualisation. The scientists observed that those times were objective indicators (markers) whose assessment had to be interpreted according to the laws of both physics and biology. Neoplasm size and location measurements may be performed also by means of other techniques of computed tomography but imaging using Nuclear Magnetic Resonance is not only the safest and the best solution for multiple use but it also permits earlier diagnosis of even preneoplastic states, which they demonstrated in their first joint work, consistently confirming the new theory of neogenesis at an atom level (Klimek *et al.* 1981a,b, 1982a,b; Mann *et al.* 1984). Thermodynamic presentation of the body takes R. Virchow's cellular theory about the structure of the system from the level of cell nucleus to atomic nucleus. Due to clinically perceptible signals of Nuclear Magnetic Resonance, for the first time it became obvious, literally *de novo*, that man is actually built of atoms, even though human senses permit perceiving only colour, sizes, motion, taste, consistency or smell of body parts. It is a huge advantage of Nuclear Magnetic Resonance that it makes it possible to identify dissipathogenic states in tissues, which can be diagnosed with other methods much later, as preneoplastic states. For instance, in 2005 increased metallothionein expression was demonstrated not only in endometrial cancer cells but also in healthy endometrial endothelium adjacent to the tumour and in cervical smooth muscles in direct vicinity of the infiltration; however the farther from the tumour the lower the expression was. This determines the spatial limits of occurrence of the dynamic genetic lesions that confirm existence of dissipathogenic space around the tumour, significant enough to be considered in the planning of therapy and in its ex juvantibus assessment. (Klimek M *et al.* 2005; Mak *et al.* 2006; Wicherek *et al.* 2005a,b, 2006).

After the surgical era, treatment of neoplasm was expanded by radiotherapy and chemotherapy. Each of those methods has strictly defined indications and contraindications and efficacy depending on the progress of science and medicine; however none of the methods initially assumed strengthening of natural immune mechanisms of the body. Even very promising chemotherapy leads in some cases to formation of a new cell clone of the existing neoplastic cells that are resistant to this treatment. This type of formation of new lines of neoplastic cells can be identified mostly through immunological processes. When compared to the cells of the body's own tissues, neoplastic cells may still produce enzymes or hormones characteristic of them, with the same or altered structure and/or function or stop their production, or synthesise entirely new biochemical compounds. These four possibilities of new cells let us imagine a too large number or antigens of neoplastic cells to manufacture drugs against them. This is why production of immunopotentialisation vaccines ought

to use the eternal coexistence of symbiotic microorganisms – because they not only cooperate with human labile cells (macrophages, leukocytes, lymphocytes and erythrocytes) but, mostly for their own existence, they eliminate pathogenic organisms from their environment [Klimek 1986, 2007a; Milovanowic 1980).

Immunotherapy, similarly to neurohormonal therapy, is a systemic treatment method against neoplasms and preneoplastic states. Two general directions for immunotherapy of neoplastic diseases arise from the thermodynamic essence of neogenesis: the direct one – targeting neoplasms, and the indirect one – leading to normalisation or sufficient alteration of the environment of the neoplasm to push it to a state that is far from the beginning of its own thermodynamic branch. Indirect immunological therapy is represented by R. Klimek's immunopotentialisation method from 1985, aiming to change the biological state of the environment of the neoplasm in which it was formed and which – according to the laws of thermodynamics – is the only environment in which it can grow and develop (Klimek 1985a, 1986, 1987a, 1988). Immunopotentialisation treatment of cervical intraepithelial neoplasia involves also the desired cooperation of symbiotic bacteria Lactobacillus vaginalis, which – to secure their own existence in the natural environment of vagina – compete with bacteria and viruses that are pathological for man. By exchanging plasmids with those, they are a natural source of antigens for activation of human immunity system, also for the protein component of viruses. For instance, dozens of HPV (human papillomavirus) types that condition neogenesis are fought by the body with the support of saprophytic bacteria like Lactobacillus vaginalis, as is proven by the high proportion of spontaneous recoveries from viral infections and even inflammations of not only cervix in women after sexual initiation. Thanks to modern technology using protein components of several viruses of human papillomavirus, first vaccines were obtained against a few selected types of papillomaviruses. The problem is that in merely ten-plus percent cervical cancer has a direct causal relationship with infections with too many existing virus and bacteria types. The scope of activity of the vaccine introduced to oncological practice by R. Klimek, which consists of coccoidal forms and inactivated whole Lactobacillus bacteria (Gynatren, Solco-Trichovac), is much broader and it uses the natural symbiosis of the physiological flora, for centuries adapting to respond to every biological pathogen, which of course includes viruses. In 1986, at the II International Symposium of Cervical Pathology and Colposcopy, R. Klimek demonstrated that: "*usually used in chronic Trichomonas vaginalis infections, by causing immunopotentialisation of the system* [the vaccine] *may become a prophylaxis and treatment method in these lesions*" (Klimek 1987a; Klimek *et al.* 1989).

In 1980s, in studies on the role of lymphokines and monokines in response to antigenic stimulation, Aleksander B. Skotnicki with his team demonstrated the impact of immunomodulators on their production and activation with mitogens of mononuclear cells of healthy and sick people with an autoimmune disease and HIV-positive, and he applied haematopoietic growth factors both in *in vitro* marrow culture and in clinical trials, using their impact on acceleration of homeostasis regeneration (Skotnicki, 1997; Skotnicki *et al.* 1999). In 1993 he commenced high-dose chemotherapy supported with transplant of autological or allogenic marrow stem cells in patients with acute leukaemias, chronic marrow leukaemia, non-Hodgkin lymphoma and Hodgkin's lymphoma, multiple myeloma, as well as solid and nodular – mostly breast – cancer. He currently uses targeted immunotherapy with monoclonal antibodies. Using an example of marrow with irreversible damage, he has presented a state-of-the-art way of treating neoplasms in general, which he has additionally documented with over 700 marrow transplants, giving many hitherto terminal patients a chance at full recovery! In year 2000 Aleksander B. Skotnicki presented the history of Cracow's haematology, from the globally pioneering works of Józef Dietl from the middle of the 19th century, Tadeusz Tempka from the period between 1928 and 1939 and Julian Aleksandrowicz from the period between 1934 and 1984 and their students, emphasising the heroic struggle of the Jagiellonian University professors for development of Polish medicine (Skotnicki, 2000). In Cracow a patient with leukaemia was diagnosed as early as in 1852, while in 1958 one of the first syngenic bone marrow transplant procedures was performed. Contemporary treatment includes chemoradiotherapy, immunotherapy and auto- and allogenic bone marrow transplantation. In 1940s, J. Aleksandrowicz substantiated the unitary theory of haematopoiesis that is the currently fully accepted origin of all blood cells from one precursor. He described the syndromes of development and disappearance of individual haematopoietic lines, along with neoplastic and symptomatic hyperplasia. He also discovered anti-inflammatory properties of nitrogen mustard (nitrogranulogen) and excluded the infectious nature of neoplastic diseases, studying the process of morphological changes in blood of a healthy person caused by intravenous injection of blood of a patient with leukaemia. In 1950s, together with his colleagues, he published works concerning pathogenesis and treatment of myeloblastic leukaemia, blood cell histogenesis, the laws governing haematopoiesis, ultrastructure of granulocytes and platelets tested using an electron microscope, as well as immunological issues in leukocytopathies and megacaryocytopathies, daily fluctuations of ribonuclease in the urine of patients with myeloid leukaemias, and treatment of leukaemias and Hodgkin's lymphoma using corticotropin. Biochemical studies on the pathogenesis of leukaemias, carried out together with B. Skarżyński's team using paper electrophoresis and electron microscopy, made it possible to divide them precisely using

comparison with granulocyte proliferation in healthy people. As early as in 1955, increased activity of nucleic acids in granulocytic leukaemia was observed and it was demonstrated that ribonuclease concentration was many times higher in the urine of sick people than in physiological states and that ribonuclease was present in leukaemia eosinocytes along with myeloperoxidase and dehydrogenase. In 1962 J. Aleksandrowicz and colleagues, based on observation of children with acute myeloid leukaemias, aplastic anaemia and generalised lymphoma, developed a concept of transplanting autological bone marrow. Simultaneous epidemiological studies indicated modern prophylaxis through identification of the impact of environmental factors on the system of people and animals, and on the relationship between the psyche and blood diseases and neoplastic processes. Finally, in 1982 J. Aleksandrowicz and A. B. Skotnicki summarised their long-term studies in the monograph *Leukemia Ecology – Ecological Prophylaxis of Leukemia* (Aleksandrowicz & Skotnicki, 1982). At the end of the 20th century, A.B. Skotnicki built from scratch a modern haematology academic centre, characterised by patients' creative participation in diagnostic and therapeutic procedures, which is best shown in book publications entitled *Multiple myeloma* (Jurczyszyn & Skotnicki, 2010, 2011) and regular meetings with people who got their lives back. In 1960, based on observations of schizophrenics, an equally prominent clinician Antoni Kępiński described a generally natural phenomenon of self-organisation of their social life, and contemporarily the school of A. B. Skotnicki gave the life of blood cells of sick people a biophysical dimension. This way a student of J. Aleksandrowicz fulfilled the dreams of his mentor about the primary significance of the environment (surroundings) for man's existence and preservation of human health, for instance when a woman cured from leukaemia gave birth to a child after successful implantation of bone marrow cells with a male genome (Hodorowicz *et al.* 2011; Jasiczek & Klimek, 2011).

THERMODYNAMIC ONCOLOGY

Histopathological test is still a certain and decisive diagnosis of a self-organising dissipative neoplastic structure at a cell level. A breakthrough in this respect involved introduction of tissue imaging with regard to matter and energy using nuclear magnetic resonance, which made it possible to study the cell metabolism of not only neoplasms, but what is much more important from medical point of view also cells in preneoplastic states. Still, the most important theoretical supplement was the Noble Prize winning (in 2005) discovery of the metathesis reaction, which explained the role of the whole system with regard to each of its components, including of course the neoplastic cell (system) transformed as a result of changes to the structure of nucleic acids (microsystems). Not only the cell cytoskeleton but also the seemingly inactive parts of the cell nucleus genome can be regarded as specific bio-catalysers, and even a possibility of nuclear DNA self-organisation may be considered (Klimek *et al.* 2006; Hodorowicz *et al.* 2011). It is medical thermodynamics that makes it possible to change the way of thinking from analytical investigations to synthesis of phenomena and to explain them in a way understandable for a wide range of people, not only for specialists. In self-organisation of cell's deoxyribonucleic acids, some nucleotides of cell nucleus (genome) as the metathesis reaction catalyser are not substituted, which is why it could have seemed that they were genes with an undetermined function (even called nonsense genes). This way, reductionism of molecular biology in the science of nuclear DNA structure came to an end, closing the dominance of supporters of solely genetic carcinogenesis in favour of participation of the whole inner state of a cell and the environment.

Scientists are under the obligation to communicate the truth about cancer according to the general state of knowledge and not only according to the views of oncologists. Over 80% of malignant neoplasms are formed with participation of carcinogens that pertain to mostly human behaviour: lifestyle, diet and behaviour connected with reproduction. The factors contained in the smoke of burnt tobacco condition malignant neoplasms not only in lungs (80–90% in men) but also in the oral cavity, throat, larynx, oesophagus, pancreas, urinary bladder and kidney, and smoking cessation significantly reduces the risk of carcinogenesis. Food components may have both harmful and protective effects, similarly to physical exercise. Among occupational factors, the highest risk concerns skin, airways, lungs and urinary bladder, but these factors apply to only ca. 5% of neoplasms in men and 1% in women. Current results of epidemiological and clinical trials – in a huge scope, which covers observations of human behaviour at work, school and during leisure in various periods of human life – were presented in the monograph *Gastrointestinal cancer in Poland* by Wiesław Jędrychowski, for years managing an international team comprised of representatives of various fields of medicine, biology, psychology and sociology (Jędrychowski, 2004; Jędrychowski & Maugeri, 2004). Their greatest value is full documentation of the frequency of occurrence of various factors determining the development of a neoplastic disease and their mutual numerical ratios. For instance, the frequency of the total impact of viruses, other infections and genetic disorders (15%) which are – also in accordance with world literature – commonly considered as oncogenic factors is lower than that of such important variables as diet (30–35%) and smoking (30–32%)! Analytical and epidemiological studies on gastrointestinal diseases showed the impact of diet, lifestyle, nicotinism and alcoholism on incidence of stomach cancer against the functioning of a whole family that was influenced by many oncological risk

factors. Similarly, the factor that plays the primary role in cervical cancer is improper procreation, as evidenced by the same oncological risk factors that lead to preterm births (Klimek M *et al.* 1999, 2002), and in women with postpartum hypothalamic dysfunction preneoplastic cervical lesions are observed in colposcopic tests in as many as 20% of cases and in cytological tests in at least 10% (Klimek 2001; Klimek & Paradysz, 1969; Klimek & Walas-Skolicka, 1977; Madej & Klimek, 1988).

In 2006, according to contemporary understanding of biological structures and processes, as wells as temporal and spatial events, in the book *Cancer – neoplasms and neoplastic diseases*, R. Klimek, J.M. Madej and A. Sieroń directly referred to the general biological scientific achievements and traditions of the Jagiellonian University on the 100th anniversary of the beginnings of modern biochemistry and physics. Having their own experience in conservative and surgical treatment and radiotherapy of neoplasms, including the use of radium, they presented the dissipative nature of cancer, discovered with Polish participation, so that everyone could – for their own good – understand the determinants behind neoplastic diseases and the primary significance of their own lifestyle in the formation and progress of these diseases, along with learning the importance of caring about the environment inhabited by people (Klimek *et al.* 2006). The text of this book includes edited parts of the monograph by R. Klimek entitled *Cancer – cause, determinants and self-defence*, of 1985, whose content as to substance remained unchanged – it was only supplemented with e.g. explanations of the reasons behind the failure of a medical procedure based on reductionist approach to genome and behind delays in clinical application of imaging and spectroscopy using Nuclear Magnetic Resonance (Klimek 1985a). Finally, in 2011, S. Hodorowicz, D. Jasiczek, R. Klimek and R. Tadeusiewicz presented contemporary oncology in a generally accessible book entitled "*Cancer and infertility. Truth and myth of medicine*", and they published the relevant source data in reputed scientific journals (Klimek 2010; Klimek *et al.* 2011, 2012).

CONCLUSION

What has proven to be the greatest disappointment in the fight against neoplasm was the discovery of its thermodynamic cause in a natural environmental phenomenon – self-organisation of biological dissipative structures. This purely biophysical cause of cancer cannot disappear as neither can the existence of equally natural phenomena like e.g. lightening. Due to meteorological forecasts, effects of this dangerous phenomenon have been largely reduced through use of constantly improved lightening conductors; still, despite the progress in knowledge, man fails to behave reasonably at all times during storms. When it comes to effective fight with cancer, the hopes focus on detecting and/or delaying the dissipathogenic states, well known as preneoplastic states, and on strengthening the natural protection of a sick body against neoplasms, e.g. via immunopotentialisation with vaccines (Klimek 1986; Bałajewicz *et al.* 1989; Klimek *et al.* 1989). Prevention, prophylaxis and proper treatment is of great significance in those who have suffered from diseases which statistically increase incidence of certain neoplasms. For instance, the following predispose a woman to cervical cancer: obstetrical haemorrhage, preterm birth, lack of lactation or diagnosed postpartum, early-age or dieting-related hypothalamic dysfunction, while improper lifestyle and diet in a family predispose people to gastrointestinal cancers (Klimek M & Klimek 1990; Klimek M *et al.* 2005a; Klimek *et al.* 1996; Smith *et al.* 2003). Special care about the health of pregnant women, through proper monitoring of foetus development, determining the time of delivery with an accuracy to days rather than weeks (Cosmi *et al.* 1997; Czajkowski, 2009; Czajkowski & Szymański, 2006; Jasiczek *et al.* 2012; Klimek M, 1996; Klimek M *et al.* 2005a,b,c; Klimek 1964, 1967, 1994, 1969) and treatment of neuroendoctrinal disorders during pregnancy using ACTH-depot therapy (Klimek M, 2005; Klimek 2000; Klimek *et al.* 2012; Klimek, Klimek, Jasiczek, 2011), as well as limitation of hormonal contraception (Cogliano *et al.* 2005; Smith, 2003; Vessey, 2006) and in vitro fertilisation (Van Leeuwen, 2011) – all this becomes particularly important.

In his book *A Passion for DNA* (Amber 2000), J. D. Watson – the co-discoverer of the DNA double helix structure in 1953 and co-initiator and first coordinator (1989–1992) of the project created to understand human genome – reminded us that in 1970s Americans devoted 10 billion dollars, without achieving the final result, to studies on cancer carried out by two competing groups of researchers with different goals, where "one wanted to cure it and the other – to understand it." In 1974 he himself thought his "long-term goal is merely to understand rather than cure cancer;" however, he considered the period from 1945 to 1965 to be a revolutionary transformation of biology from descriptive science to powerful analytical science as a result of taking advantage of biologists' tendency to descriptions if they were taught the rudiments of contemporary physics and chemistry. Before that, between 1941 and 1945, a Pole B. Skarżyński and a German H. von Euler-Cheplin published works summarising the biochemistry of neoplasms and they were right to indicate e.g. the significance of genes in carcinogenesis, with genes perceived by them according to more modern notions than those currently expressed in biochemistry, where they are reduced just to a sequence of nucleotides (von Euler-Cheplin & Skarżyński, 1942). People are most effectively protected against self-organisation of neoplasms by living according to autoteological principles, which means that man acts in accordance with their own and socially acceptable ethical and moral values (Fedor-Freybergh, 1988, 1992; Hodorowicz *et al.* 2011; Jasiczek & Klimek, 2011; Klimek 2012).

At a level of thermodynamic deliberations, we may compare such different carcinogenic factors as e.g.: viruses, gene mutations, ultraviolet radiation, ageing, diet components and the type and time of physical exercise, or even the height and age of man. Eventually, a purely information-related disease was described in people – informatosis; it involves a social form of life that entirely bends a sick man to its rules (Klimek 2012). There are many reasons required for each system (not only a biological cell) to be brought to dissipathogenic states which would inevitably endanger its existence; this – even though very rarely – may or even must lead to self-organisation of its components into a more efficient system, provided that this new creation increases dissipation of matter and energy in its environment. It is this dissipation that causes the signs and symptoms of neoplastic diseases ending with destruction of the body if the treatment comes too late and/or is insufficient, limited only to removal of neoplastic lesions without the always necessary elimination and/or prevention of preneoplastic (dissipathogenic) states. Every disease is only one of the many unhappy events in the life of man, who is always influenced by social determinants. It is why an oncological strategy must begin with direct destruction of the neoplasm whose clones cause the neoplastic disease rather than with actions taken at the stage of existing symptoms and signs of neoplastic diseases. It was the discovery of the dissipative structure of neoplasm that made it possible to understand the apparent differences between the views on the etiopathogenesis and treatment of neoplastic diseases.

REFERENCES

1 Aleksandrowicz J, Skotnicki AB (1982). Leukemia Ecology – Ecological Prophylaxis of Leukemia. NIH Bethesda USA.
2 Bałajewicz M, Dembowska J, Klimek R (1989). Test of immunopotentialization in colposcopy – a clinical evaluation. Eur J of Obstet and Gynecol and Reprod. Biology. **33**: 253–257.
3 Cogliano V, Grosse I, Baan R. Straif K, Secretan B (2005). Carcinogenicity of combined oestrogen-progestern contraceptives and menopausal treatment. Lancet Oncol. **6**: 552–553.
4 Cosmi EV, Klimek R, Di Renzo GC, Kulakov V, Kurjak A, Maeda K *et al.* (1997). Prognosis of birth term: recommendations on current practice and overview of new developments. Archives of Perinatal Medicine. **3**(2): 31–50.
5 Czajkowski K (2009). Dysypatywna etiologia nowotworów. [(Dissipative etiology of neoplasms.) (In Polish)] Alma Mater. **110–111**: 84–86.
6 Czajkowski K, Szymański W. editors (2006). Rudolfa Klimka Położnictwo. [(R.Klimek's Obstetrices.) (In Polish)] RK Kraków
7 Fedor-Freybergh PG (1988). Prenatal and Perinatal Psycho-Medicine. Encounter with the Unborn. The Parthenon Publishing Group Ltd Carnforth, New Jersey
8 Fedor-Freybergh PG (1992). Prenatal and Perinatal Psycho-Medicine in changing word. In: Klimek R, editor Psycho-Medicine Cracow. p. 50–55.
9 Hodorowicz S, Jasiczek D, Klimek R, Tadeusiewicz R (2011). Rak i niepłodność. Prawda i mity medycyny. [(Cancer and infertility. Truth and myth of medicine.) (In Polish)]. Trio Kraków-Warszawa.
10 Jasiczek D, Klimek R (2011). Życie i medycyna [(Live and medicine.) (In Polish)]. Hermes Management S.A.
11 Jasiczek D, Klimek R, Stencl J, Tadeusiewicz R, Tholt M (2012). Obstetrical prevention of human cancers. Neuroencrinology Letters. **33**(2): 118–23.
12 Jędrychowski W editor (2004). Gastrointestinal cancer in Poland. Jagiellonian University Press.
13 Jędrychowski W, Maugeri U (2004). Contribution of epidemiology in Poland to better understanding of the natural history of gastrointestinal tract diseases. European Epi Marker. **8**(3): 1–7.
14 Jurczyszyn A, Skotnicki AB, editors (2010). Szpiczak Mnogi. [(Multiple myeloma.) (In Polish)] WM Wrocław.
15 Jurczyszyn A, Skotnicki AB, editors (2011). Szpiczak Mnogi. t.II. [(Multiple myeloma, v.II) (In Polish)]. Fundacja MM Kraków.
16 Kaim I, Klimek M, Popiela TJ (2001). 60-lecie epoki biochemii nowotworów. [(60-years of neoplasm biochemistry.) (In Polish)] Gin Prakt. **9**: 32–34.
17 Kaim I, Klimek R, Migdał M (2005). Neuroendokrynne dojrzewanie kobiet a prokreacja i neogeneza. [(Neuroendocrinological woman's maturation and the procreation and neogenesis) (In Polish)]. Gin Prakt. **4**(85): 2–5.
18 Klimek M (1996). Monitowanie ciąży i prognozowanie porodu jako zdarzeń czasoprzestrzennych. [(Monitoring of pregnancy and prognosis of birth as time-space events.) (In Polish with English summary)] UJ DREAM Kraków.
19 Klimek M (2005). Comparative analysis of ACTH and oxytocinase plasma concentration during pregnancy. Neuro Endocrinol Lett. **26**: 337–341.
20 Klimek M, Klimek R (1990). Cervical intraepithelial neoplasia after high-risk pregnancy. Gin Pol. **61**: 575–577.
21 Klimek M, Klimek R, Mazanek-Mościcka M (1999). Biological diagnosis and prognosis in practical obstetrics. Polish J Gynaec Invest. **2**(2): 57–66.
22 Klimek M, Klimek R, Mazanek-Mościcka M (2002). Preterm birth as an indicator of cancer risk for the mother. It J Gynacol Obstet. **3**: 73–77.
23 Klimek M, Pabian W, Tomaszewska B, Kołodziejczyk J (2005a). Levels of plasma ACTH in men from infertile couples. Neuro Endocrinol Lett. **26**: 347–350.
24 Klimek M, Wicherek Ł, Gałązka K *et al.* (2005b) Cycle dependent expression of endometrial metallothionein. Neuro Endocrinol Lett. **26**: 663–666.
25 Klimek M, Wicherek L, Popiela TJ, *et al.* (2005c). Changes of maternal ACTH and oxytocinase plasma concentrations during the first trimester of spontaneous abortion. Neuro Endocrinol Lett. **26**: 342–346.
26 Klimek R (1964). Pregnancy and labor in terms of studies on the oxytocin-oxytocinase system. Folia Med Cracov **6**: 471–482; In: Klimek R, Król W, editors. Oxytocin and its analogous. Cracow: PTE.
27 Klimek R (1967). Relative duration of human pregnancy and oxytocin therapy. Gynecologia. **163**: 48–55.
28 Klimek R (1994). Monitoring of pregnancy and prediction of birth date. The Parthenon Publishing Group, New York, London.
29 Klimek R, Drewniak K, Bieniasz A (1969). Further studies on the oxytocin-oxytocinase system. Am J Obstet Gynecol. **105**: 427–430.
30 Klimek R (1978a). Dysypatywna struktura nowotworów na modelu raka szyjki macicy. [(Dissipative structure of neoplasms, studies on the model of uterine cervix cancer.) (In Polish)]. Gin Pol. **49**: 765–769.
31 Klimek R (1978b). Hypothalamus hypofunction as an etiological factor in cervical neoplasia. Abstracts of III World Congress I.F.C.P.C. 20, Orlando.
32 Klimek R (1980). Neuroendocrinologic aspects of the dissipative struktures of tumors. Mat Med Polona. **1–2**: 91–96.
33 Klimek R (1982). Nucleomagnetic resonance of atoms as an evidence of dissipative structure of malignant tumors. Przegl Lek. **39**: 313–317.
34 Klimek R (1983). Etiopathogenesis of tumors and theories of oncogenesis. Gin Pol. **54**: 603–609.
35 Klimek R (1985a). Rak – przyczyna, uwarunkowania i samoobrona. [(Cancer – cause, determinads and host-defense.) (In Polish with long English summary)] PWN Warszawa.

36 Klimek R (1985b). Neuroendokrynologiczne i ginekologiczne uwarunkowania kancerogenezy. [(Neuroendocrinologic and gymecologic condicions of cancerogenesis.) (In Polish with English abstrect)] Mat Jubil Zjazdu PTG Kraków. t.I. 11–18.
37 Klimek R (1986). Immunotherapy of cervical intraepithelial neoplasia. In: Bompiani A, Carenza L, Salvadori B, Pachi A, editors. LXIV Congresso Nazionale della Societa Italiana di Ginecologia e Ostetrica. **vol.I**, 275–278.
38 Klimek R (1987a). Indukcja i stymulacja immunologicznej samoobrony Gynatrenem (Solco Trichovac) jako przykład przyczynowej profilaktyki i leczenia nowotworów. [(Induction and stimulation of immunological self-defence by Gynatren as an example of causing prophylaxis and treatment of neoplasms.) (In Polish with English anstract)] Gin Pol. **58**: 552–555.
39 Klimek R (1987b). NMR imaginig in terms of human atomic patology. Europ J ObstetGyn & Reproductive Biology. 24(2): 135–143.
40 Klimek R (1988). Immunopotencjalizacja w profilaktyce i leczeniu śródnabłonkowej neoplazji szyjki macicy. [(Immunopotencialization in the prophylaxis and treatment of intraepithelial neoplasia of uterine cervix.)(In Polish)] I Konferencja Naukowa Polskiego Towarzystwa Onkologicznego Bydgoszcz, 19–20, XI; Nowotwory, str. 55–60.
41 Klimek R (1990a). Cervical cancer as a natural phenomenon. Eur J Obstet Gynecol Reprod. Biol. **36**: 221–238.
42 Klimek R (1990b). Nuclear magnetic resonance in obstetrics and gynecology. Int J Gynecol Obstet. **32**: 199–205.
43 Klimek R (1990c). Conquering cancer ourselves. New trends in gynecology and obstetrics. J.Libbey CIC s.r.l., Roma **Vol. VI** No 2: 53–117.
44 Klimek R (1990d). Casual prevention of cancer as a natural biological phenomenon. Medicine Biologie Environment. **18**: 8–10.
45 Klimek R (1992). Prevention of cervical cancer promotion in gynecological practice. III Sympozjum of Cervical Pathology. Kraków p. 129–133.
46 Klimek R (2000). Enzymes: The most important markers of pregnancy development. J Early Pregnancy. **4**: 219–229.
47 Klimek R (2001a). Biology of Cancer: Thermodynamic Answers to Some Questions. Neuroendocrinology Letters. **22**: 413–416.
48 Klimek R (2001b). The use in obstetrics of quantum theory as well as modern technology to decrease the morbidity and mortality of newborns and mothers during iatrogenic induced delivery. Neuroendocrinology Letters. **22**: 5–8.
49 Klimek R (2001c). Precancerous and cancerous states in the light of the modern knowledge. Kolposkopia. **1**(1): 41–42.
50 Klimek R (2004). The etiology of cancer in historical view. Ginekol Onkol. **2**(4): 214–222.
51 Klimek R (2007a). Profilaktyczno-terapeutyczne szczepienie przeciwko stanom przedrakowym szyjki macicy. [(Prophylactic and therapeutic vaccination against precancerous states of uterine cervix.) (In Polish with English abstract)] Gin Prakt. **15**(2): 36–40.
52 Klimek R (2007b). Cell as a biological form of life. Ginekol i Położn. **3**(5): 9–17.
53 Klimek R (2010). Cancer: health hazard resulting from attempted life protection. Curr Gynecol Oncol. **8**(3): 149–159.
54 Klimek R (2012). Dekalog jako teologiczny program Świętej Trójcy w stworzeniu świata. [(Ten Commandments – Holy Trinity teleological program of the universe creation)(In Polish with English abstract)] In: Jamrozy M, Kuźmicz A, Wszołek B, editors, Człowiek i Wszechświat. 59–68.
55 Klimek R, Bręborowicz GH, Chazan B, Czajkowski K, Dębski R, Dubcak J, Fedor-Freybergh P *et al.* (2001). Declaration of the Childbirth in XXI century. Archives of Perinatal Medicine. **7**(3): 8–14; Gin Prakt. **9**: 6–13; Gin Pol. **73**: 3–13.
56 Klimek R, Dembowska J, Bałajewicz M, Plechanow J (1989). Effect of immunopotentialization on rate of vaginal smear normalization according to appearance of cervical intraepithelial neoplasia. Int J Gynecol Obstet. **28**: 41–44.
57 Klimek R, Fedor-Freybergh PG, Walas-Skolicka E (1996) A Time to Be Born. DREAM Cracow.
58 Klimek R, Jasiczek D, Gralek P, Fedor Freybergh P (2011). Cancer – final cellular form of life. Int J Prenat Psychol Medicine. **23**: 1–2: 7–17.
59 Klimek R, Kaim I, Jaskulska B, Dziechciowski M (1999). Medycyna za zamkniętymi drzwiami. [(Medicine behind the closed doora.) (In Polish)] DREAM, Kraków.
60 Klimek R, Klimek M, Gralek P, Jasiczek D (2012). Causal ACTH-depot therapy during pregnancies following infertility treatment. Obstetrics Gynecology International. **Volume 2012**, article ID 248926, 7p
61 Klimek R, Klimek M, Jasiczek D (2011). Immunotherapy of cervical cancer as a biological dissipative structure. Neuroendocrinology Letters. **32**(4): 380–388.
62 Klimek R, Lauterbur PC, Mendonca-Dias MH (1981a). A discussion of nuclear magnetic resonance (NMR) relaxation time of tumors in terms of their interpretation as self-organising dissipative structures and of their study by NMR in vivo by NMR zeugmatographic imaging. Gin Pol. **52**: 493–502; Materia Medica Polona. **15/119**: 47–53.
63 Klimek R, Lauterbur PC, Mendonca-Dias MH (1981b). Nukleomagnetyczny rezonans w diagnostyce i terapii ginekologicznej. [(Nucleomagnetic resonance in gynecological diagnosis and therapy.) (In Polish with English abstract)] XXI Congress PTG Poznań. t.II: 27–28.
64 Klimek R, Lauterbur PC, Mann WJ, Mendonca-Dias MH, Kaplan C (1982a). Nuclear resonance technique in human surgery. Przegl Lek. **39**: 335–338.
65 Klimek R, Lauterbur PC, Mendonca-Dias MH *et al.* (1982b). Nuclear magnetic resonance relaxation time as a proof of the plasmid in Escherichia Coli. Przegl Lek. **39**: 533–534.
66 Klimek R, Loster A, Dembowska J, Bałajewicz M (1986). CIN as an indication for immunotherapy with Gynantren. 2nd Symposium of Study Group for Cervical Pathology and Colposcopy. Cracow-Rabka. 158–162,
67 Klimek R, Madej J (1964). Octapressin in colposcopy. In: Klimek R, Król W, editors: Oxytocin and its analogues. Cracow Sympozjum PTE, p.115–118; Gin Pol. **35**: 290–294.
68 Klimek R, Madej J (1985). Równoczesność zmian nabłonkowych i naczyniowych w kancerogenezie. [(Simultaneous appearance of epithelial and vascular changes in cancerogenesis.) (In Polish with English abstract)] Gin Pol. **56**: 53–56.
69 Klimek R, Madej JM, Sieroń A (2006). Rak – nowotwory a choroby nowotworowe. [(Cancer – neoplasms and neoplastic diseases.) (In Polish)]. RK Kraków.
70 Klimek R, Paradysz A (1969). Współistnienie zespołu podwzgórzycy pociążowej z rakiem szyjki macicy. [(The co-existence of the post gestational hypothalamosis with the cancer of uterine cervix.) (In Polish with English abstract)] Gin. Pol. **40**: 125–129.
71 Klimek R, Pawlikowski M (1973). Neuroendokrynologia kliniczna. [(Clinical neuroendocrinology.) (In POlish)] PZWL Warszawa.
72 Klimek R, Skarżyński B, Szczepkowski TW (1956). Cytochrom w Thiobacillus thioparus. Biochemistry of autotrophic sulphuric bacteria. Acta Biochem.Pol. **3**: 261–266.
73 Klimek R, Walas-Skolicka E (1977). Le syndrome hypothalamique post-gravidique comme agent de risque de developpement de cancer du col uterin. Arch Anat Cytol Path. **25**(5): 305–309.
74 Madej J, Klimek R (1988). Obserwacje kolposkopowe rezultatów immunopotencjalizacji w obrębie szyjki macicy. [(Colposcopic observations of the results of immunopotentialization within the uterine cervix.) (In Polish with English abstract)] Gin Pol. **59**: 147–150.
75 Mak P, Wicherek L, Suder P. *et al.* (2006). Analysis of free hemoglobin level and hemoglobin peptides from human puerperal uterine secretions. J Soc Gynecol Invest. **13**(4): 285–91.
76 Mann WJ, Mendonca-Dias MH, Lauterbur PC, Klimek R (1984). Preliminary in vitro studies of nuclear magnetic resonance relaxation time and three-dimensional nuclear magnetic resonance imaging in gynecological oncology. Am J Obst Gynec. **148**: 91–96.
77 Milovanowic R, Grcic R, Stojkovic L (1980). Effect of vaccination with SolcoTrichovac on the vaginal flora of female patients with Trichomoniasis. Biol Res Pregnancy. **1–4:** 181–186.
78 Prigogine I (1980). From being to becoming: time and complexity in the physical science. San Francisco W.H.Freeman.

79 Skarżyski B, Klimek R, Szczepkowski T (1956). Cytochrom in thiobacillus thioparus. Bull Pol Acad Science. **4**: 299–302.
80 Skotnicki AB (1997). Zastosowanie hematopoetycznych czynników wzrostu (CSF) w praktyce klinicznej. [(In Polish)] Acta Haematol Pol. **28**,(Supl 2): 59–62.
81 Skotnicki AB (2000). Historia Krakowskiej Hematologii. [(History of Cracow Haematology.) (In Polish with English abstrakt)]. Przegląd Lek. **57**: 7–16.
82 Skotnicki AB, Zawirska D, Nowak W (1999). Ogólna charakterystyka, podstawy i procedury wysoko dozowanej chemioterapii wspomaganej przeszczepieniem macierzystych komórek krwiotwórczych. [(General characteristics, bases and high dose chemotherapy procedures supported by stem cell transplantation.) (In Polish with English abstract)] Przegl Lek. **56**: 10–21.
83 Smith JS, Green J, Berrington de Gonzalez A, *et al.* (2003). Cervical cancer and use of hormonal contraceptives: a systemic review. Lancet. **361**: 1159–1167.
84 Smoluchowski M (1906) Zur kinetischen Theorie der Brownschen Molekularbewegung und der Suspensionen. Ann Phys. **21**: 756–780.
85 Van Leeuwen FE, Klip H, Mooij TM *et al.* (2011). Risk of borderline and invasive ovarian tumors after ovarian stimulation for in vitro fertilization in a large Dutch cohort. Hum Reprod. **26**(12): 3456–3465.
86 Vessey M, Painter R (2006). Oral contraceptive use and cancer. Findings in a large cohort study, 1968–2004 Br J Cancer. **95**: 385–389.
87 von Euler-Cheplin H, Skarżyski B (1942). Biochemie der Tumoren. F.Enke Verlag Stuttgart.
88 Wicherek L, Gałązka K, Popiela TJ. *et al.* (2006). Metallothionein expression and infiltration of cytotoxic lymphocytes in uterine and tubal implantation site. J Reprod Immunol. **70**: 119–131.
89 Wicherek L, Klimek M, Dutsch-Wicherek M (2005a). The level of maternal immune tolerance and fetal maturity. Neuro Endocrinol Lett. **26**: 561–566.
90 Wicherek L, Popiela TJ, Gałązka K. *et al.*(2005b). Metallothionein and RCAS1 expression in comparison to immunological cells activity in endometriosis, endometrial adenocarcinoma and endometrium according to menstrual cycle changes. Gynecologic Oncology. **99**(3): 622–630.